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ORIGINAL PAPER

Monitoring Photochemical Reactions in Single Crystals by X-ray Diffraction: Practical Aspects

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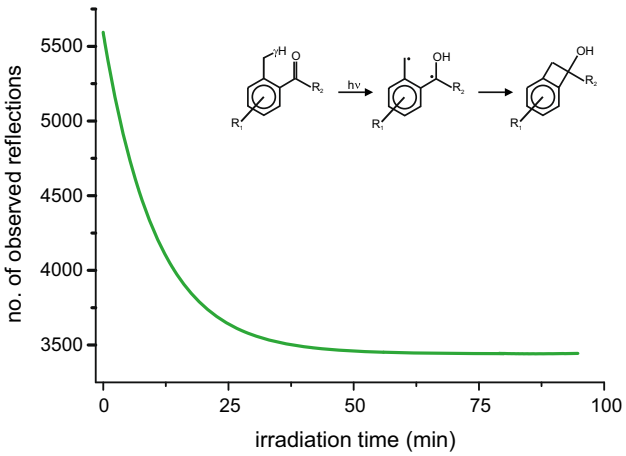
Abstract The influence of external stimuli on the decrease of crystal diffracting power and hence the quality of diffraction patterns and determined structures was studied in the case of the Norrish-Yang photochemical reaction of methyl 2-{[4-(2,4,6-triisopropylbenzoyl)benzoyl]amino}-3-phenylpropanoate, compound **1**. The reaction was conducted in a single-crystal-to-single-crystal homogeneous manner. The calculated rate constant at 75 °C was 1.6×10^{-3} s^{-1}. In a quantitative way we illustrated a relationship between the reduction of the crystal diffracting power and the content of reactant molecules in the crystal and quantitatively showed that reactant molecules are responsible for this reduction. We observed that there is no correlation between the energy of UV–vis radiation applied to induce the photochemical reaction and the degree of the decrease of crystal diffracting power. We also showed in the case of the studied crystals that some change in temperature does not influence the degree of the decrease of the crystal diffracting power under the influence of UV–vis radiation. The unknown structures of the crystals containing pure reactant and product for compound **1** were also presented.

Graphical Abstract The influence of different external stimuli on the reduction of diffracting power of crystals was monitored quantitatively during and after the Norrish-Yang photochemical reaction.



Keywords X-ray diffraction · Crystal structure · Crystalline state chemistry · Disorder · Kinetics

Introduction

When photochemical reactions in single crystals and structural transformations brought about by such reactions are monitored by X-ray diffraction, it is crucial to have crystal structures of high quality which depends on the quality and intensity of reflections collected for crystals. When we analyzed our X-ray data and also data available in scientific literature, we noticed that for many compounds the common feature is a certain decrease of a number of observed reflections, i.e. reflections of intensity $I > 2\sigma(I)$, with time of irradiation of crystals by a UV–vis beam and with the progress of a photochemical reaction. In turn, such a decrease indicates that crystal diffracting power and translational order also decreases along with the progress

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of a photochemical reaction. However, in scientific literature very little attention is paid to this phenomenon, contrary to analysis of structures of reacted or partly reacted crystals; most often this subject is neglected in discussions. To the best of our knowledge, there are only three papers in which relationships between the decrease of crystal diffracting power and crystal structures were analyzed [1–3], but each of the compounds presented in these papers were studied for only one set of external conditions.

In the research presented in this paper, we induced a photochemical reaction in crystals of one compound applying different conditions of photochemical induction, namely, various energies of a UV–vis beam and various temperatures. The decrease of crystal diffracting power was monitored step-by-step by means of X-ray diffraction and X-ray structure analysis. As the studied compound methyl 2-{[4-(2,4,6-triisopropylbenzoyl)benzoyl]amino}-3-phenylpropanoate was chosen, compound **1**, of which crystals lose diffracting power under the influence of UV–vis radiation. On the grounds of the results described in the present paper, some advice on how to conduct photochemical reactions in crystals monitored by X-ray diffraction will be given.

Experimental

Compound **1** was prepared according to the procedures reported by Ito et al. [4] and recrystallized from ethanol. Crystals were irradiated using an Hg 100 W lamp equipped with a water filter and glass filters GG420, BG39 or WG320. The transmittance of the filters is presented in Fig. 1. The total time of irradiation by GG420 was 0, 210, 270, 390, 600, 870, 1200, 2340, 3540 and 4620 min for crystal 1; by BG39 at ambient temperature: 0, 10, 20, 40, 60, 90, 120 and 150 min for crystal 2; by BG39 at 75 °C: 0, 10, 30, 50 and 80 min for crystal 3 and by WG320: 30, 45, 60, 120 and 180 min for crystal 4. The calculations of the beam penetration depth showed that for the region of the absorption maximum almost all radiation would be absorbed in the first 0.09 mm crystal layer. Therefore, we applied the beam of longer wavelengths and less absorbed by reactant molecules, which ensured the satisfactory crystal penetration and homogeneity of the transformation. After each irradiation the X-ray data were collected using a diffractometer equipped with a CCD EOS detector [5]. The reaction was carried out in a single-crystal-to-single-crystal manner. For the crystal irradiated at 75 °C the crystal structures were determined. The final refined values of the site occupation factors [6, 7] revealed the following content of the product in the crystal: 0, 61.7(11), 87.2(11) and 100.0 % for 0, 10, 30 and 50 min, respectively (the mean values calculated on the grounds of the content for both symmetrically independent product molecules C and D).

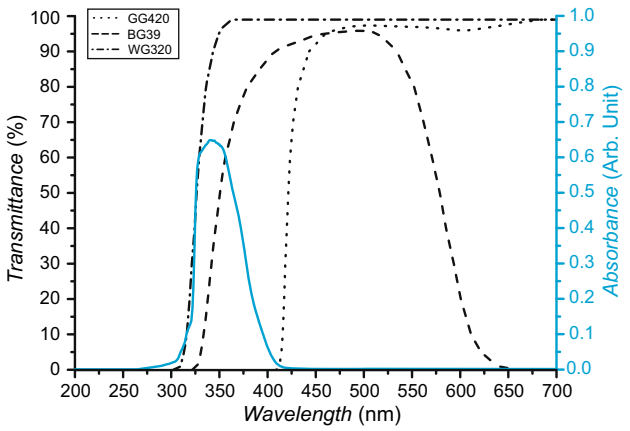


Fig. 1 The characteristics of the applied glass filters and the absorption spectrum of the studied compound

For the crystal structure of pure reactant and product, all non-hydrogen atoms are refined anisotropically. In the case of the partly reacted crystals, the major component was refined anisotropically and the minor component isotropically. The benzene rings C8 → C13 and C28 → C33 were treated as rigid rotating groups for the partly reacted crystals. Most H atoms were positioned geometrically and treated as riding with C–H = 0.93–0.96 Å and U_{iso}(H) = 1.5 U_{eq}(C) for methyl H atoms or 1.2 U_{eq}(C) for other H atoms. The H atoms at C26 in the pure reactant crystal were located in difference Fourier maps and refined as a part of a rigid rotating group. The hydrogen atom of the hydroxyl group was omitted. Owing to the reactant-product disorder, geometric restraints were applied: DFIX, DANG and SIMU [7]. The target values were taken from the structures of the pure reactant and the product crystal. Selected experimental and crystallographic data are given in Table 1. CCDC files 1063546, 1063547, 1063548 and 1063549 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

The crystals of compound **1** were not sensitive to X-rays, however, they showed a decrease of intensities of reflections owing to UV–vis irradiation. It should be emphasized that the crystals did not change their external appearance, i.e. transparency, color, shape and size and they did not crack during irradiation.

Results and Discussion

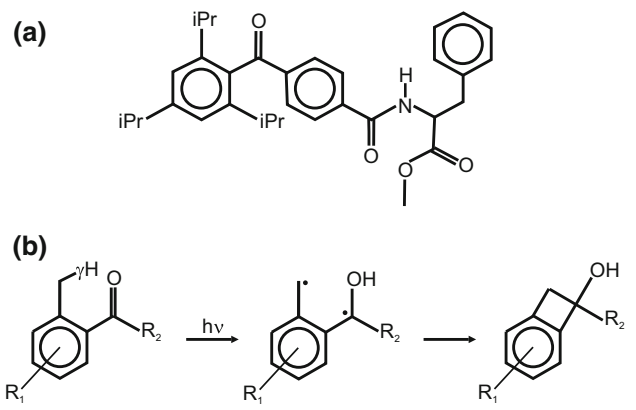
The chemical formula of the studied compound **1** and the equation of the photochemical Norrish-Yang reaction [8] which takes place in the crystals of this compound are

Table 1 Crystal and experimental data for compound **1**

	0 % P	61.7 % P	87.2 % P	100 % P
Chemical formula	$C_{33}H_{39}NO_4$	$C_{33}H_{39}NO_4$	$C_{33}H_{39}NO_4$	$C_{33}H_{39}NO_4$
Formula weight	513.65	513.65	513.65	513.65
Data collection temperature (K)	299	299	299	299
UV–vis irradiation temperature (K)	348	348	348	348
Radiation	Mo Kα	Mo Kα	Mo Kα	Mo Kα
Wavelength (Å)	0.71073	0.71073	0.71073	0.71073
Crystal size (mm)	0.40 × 0.35 × 0.10	0.40 × 0.35 × 0.10	0.40 × 0.35 × 0.10	0.40 × 0.35 × 0.10
Crystal system	Orthorhombic	Orthorhombic	Orthorhombic	Orthorhombic
Space group, Z	$Pna2_1$, 8	$Pna2_1$, 8	$Pna2_1$, 8	$Pna2_1$, 8
a (Å)	22.1785(6)	22.3090(8)	22.2416(15)	22.2498(12)
b (Å)	9.4268(3)	9.3922(3)	9.3106(4)	9.3021(4)
c (Å)	29.0789(10)	29.1878(13)	29.4803(19)	29.4831(16)
V (Å^3)	6079.6(3)	6115.7(4)	6104.9(6)	6102.1(5)
D_{calc} (Mg m^{-3})	1.122	1.116	1.118	1.118
Absorption coefficient μ (mm^{-1})	0.07	0.07	0.07	0.07
θ_{max}(°)	26.0	26.0	26.0	26.0
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	15286, 8309, 5592	15437, 8342, 4282	15359, 8314, 3539	15346, 8306, 3499
No. of parameters	687	895	766	685
R_{int}	0.035	0.041	0.047	0.047
R [$F^2 > 2\sigma(F^2)$], $wR(F^2)$, S	0.066, 0.146, 1.06	0.082, 0.194, 1.03	0.096, 0.224, 1.05	0.101, 0.245, 1.04
$(\Delta\rho)_{max}$, $(\Delta\rho)_{min}$ (e Å^{-3})	0.22, −0.17	0.19, −0.13	0.20, −0.14	0.21, −0.15

shown in Scheme 1. The reaction proceeds in two steps. In the first step, under the influence of UV–vis radiation, a γH atom is abstracted and transferred to an O atom in a carbonyl group and this leads to the formation of 1,4-hydroxybiradical. In the second step, a cyclobutane ring is created from the biradical.

For compound **1**, we determined crystal structures containing 0, 61.7, 87.2 and 100 % of the product. These structures were not published previously. Two of them are presented in Fig. 2. In Ref. [2] we presented crystal structures for this compound containing 17, 20, 26, 40 and 46 % of the product (the mean values for two symmetrically independent molecules).



Scheme 1 **a** The formula of the studied compound and **b** the equation of the photochemical reaction proceeding in crystals

The examined crystals were irradiated in steps by UV–vis radiation filtered through different glass filters transmitting different ranges of wavelengths. The characteristics of the filters were shown in Fig. 2. The energy of the transmitted UV–vis radiation changes in the following order: GG420 < BG39 < WG320. Figure 3 shows the degree of decrease of the diffracting power of the crystals (described by the decrease of a number of observed reflections) under the influence of radiation filtered by different filters. Several features can be discussed on the grounds of this figure.

Firstly, the decrease of an initial number of observed reflections is not correlated with the energy of the applied UV–vis radiation. Enkelmann et al. [10, 11] advised using wavelengths from a low energy absorption tail in order to induce photochemical reactions in crystals, which helps to conduct transformations in a homogeneous way, i.e. with uniform arrangement of reactant and product molecules which is shown in Scheme 2. However, such a range of wavelengths does not prevent crystals from the decrease of diffracting power resulting from the increase of a disorder

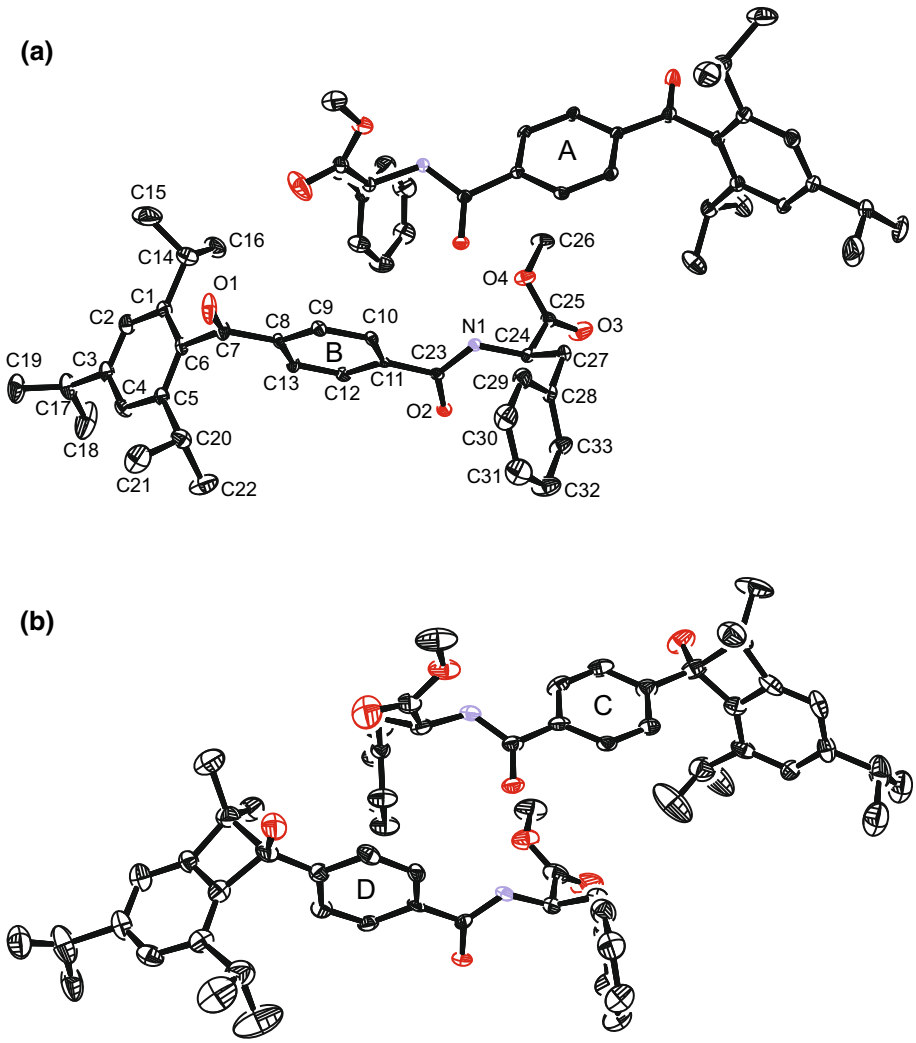
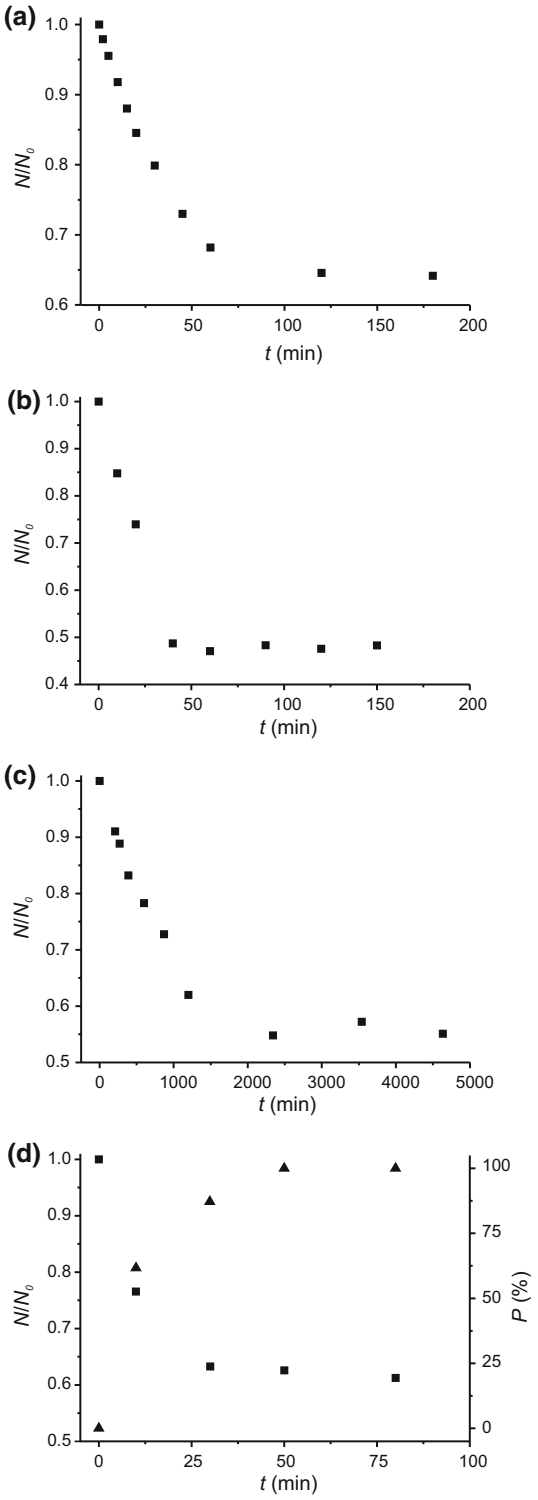


Fig. 2 Molecules in the crystal of **a** a pure reactant and **b** product visualized by means of the Ortep program [9]. Hydrogen atoms were omitted for clarity

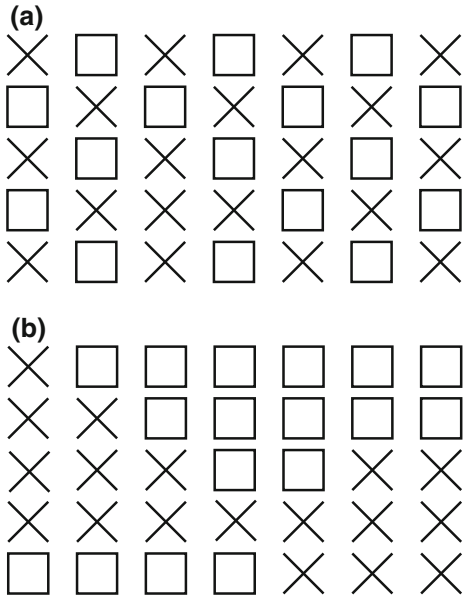
of molecules in crystals [12, 13]. It is worth mentioning that a decrease of diffracting power is commonly met for macromolecular crystals under the influence of synchrotron X-ray radiation used during data collection. However, the reasons for that decrease are connected with extremely intense and energetic beams [14, 15] and are not connected with photochemical reactions brought about by UV–vis radiation.

Secondly, the rate of photochemical reaction is correlated with the energy of the applied beam. The bigger energy, the faster the photochemical reaction is. There are known photochemical reactions which proceed in crystals in a homogeneous way independently of applied energy of UV–vis radiation (but the energy in the range of wavelengths for an absorption spectrum of a given compound) [16, 17], including compound **1** studied in this paper. Taking into account the above two features, we can advise the use of a higher energy beam for such compounds. It will not decrease a crystal's diffracting power and quality of determined structures in a higher degree, but will speed up the rate of photochemical reactions, which is important in the case of reactions proceeding very slowly.

Thirdly, after the prolonged irradiation of crystals of compound **1**, the number of observed reflections assumes a constant level, which means that the crystals stopped losing their diffracting power. We correlated the course of the decrease of crystal diffracting power with structural changes in crystals, namely, with the percentage content of the product molecules in the crystals (Fig. 3d) and with the changes in the cell constants (Fig. 4). As can be seen, the crystal diffracting power stopped decreasing when the cell constants stopped changing and when 100 % of the product was reached in the photochemical reaction. This is a nice quantitative illustration showing that the reactant molecules and their reaction to UV–vis radiation are responsible for the decrease of crystal translation order and the decrease of crystal diffracting power. To our knowledge this is the first example presenting quantitatively the relationship between the degree of a translational order (connected with a number of observed reflections) and progress



◀**Fig. 3** The decrease of the initial number of observed reflections [i.e. having an intensity $I > 2\sigma(I)$] collected after the irradiation of the crystals by the UV–vis beam filtered by **a** WG320, **b** BG39 and **c** GG420 glass at 26 °C and **d** BG39 at 75 °C together with time of the irradiation. The data for the first six points for WG320 were taken from Ref. [2] and the data for the remaining points for WG320 come from our archives and were not published previously. All the data for the remaining filters come from the present studies. In plot **d** the content of the product molecules in the crystal was presented by triangles



Scheme 2 The difference between **a** homogeneous and **b** heterogeneous transformations in crystals

of the photochemical reaction (connected with the time of UV–vis irradiation and the content of product molecules in a crystal). This illustration can be compared with the crystal behavior observed by us for two other compounds, which did not give the product of a photochemical reaction [1, 3]. In their cases, the decrease of crystal diffracting power was observed during the whole UV–vis irradiation process until the total loss of reflections. This can be understood, since during irradiation there were always reactant molecules interacting with UV–vis radiation.

Fourthly, there is no influence observed of temperature on a decrease of crystal diffracting power and translational order in the case of the studied compound and the applied experimental conditions. A similar decrease is observed for irradiation carried out at 75 and 26 °C. However, there is a significant increase of reaction rate with the increase of temperature. An increase of temperature is not always connected to an increased rate of photochemical reactions in crystals. For instance, the decrease of reaction rates was observed in the case of [2 + 2] dimerization and was a consequence of molecular motions, which disabled an overlap of *p*-orbitals and formation of bonds [18].

The decrease of the number of observed reflections for the studied compound (see Fig. 3) can be correlated with mosaicity: the mosaicity increases as long as the number of observed reflections decreases. For instance, for the

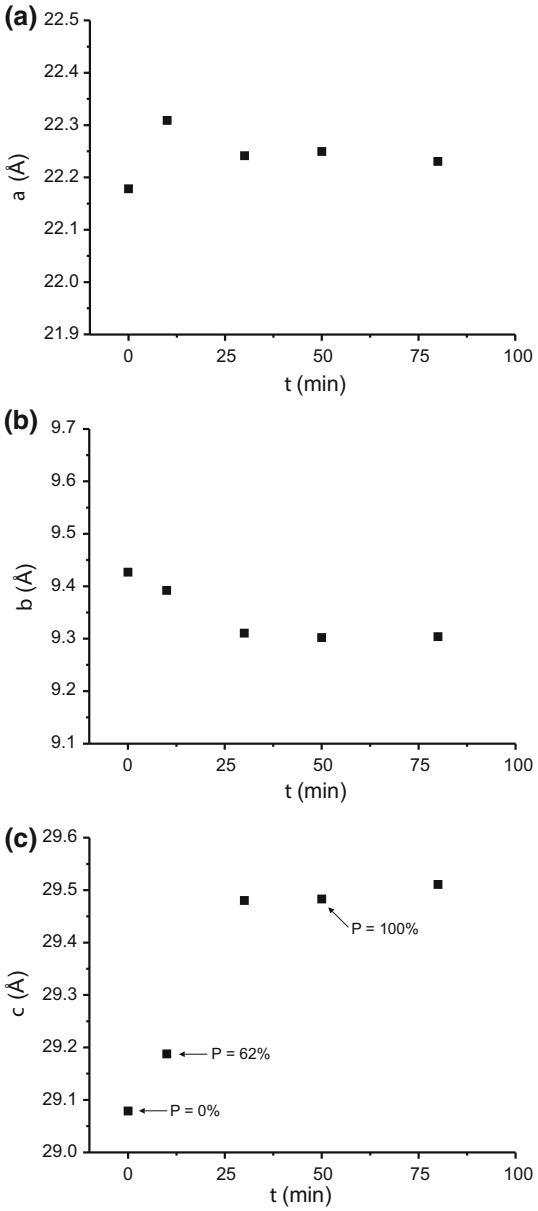


Fig. 4 The changes in the cell constants with the time of the UV–vis irradiation of the crystal using filter BG39 at 75 °C

WG320 filter the average mosaicity changes from 0.78° to 1.00° and then remains constant.

When a crystal is selected for monitoring a course of photochemical reactions by single crystal X-ray structure analysis, two other aspects should also be taken into account. Both of them are connected with the size of a single crystal. The crystal should give a diffraction pattern of good quality. Among other things, a ratio between a number of observed reflections and refined parameters should be sufficiently high: the bigger the ratio, the better it is. This would mean that crystals which are too small should not be selected. However, a second aspect should also be taken into account: homogeneity of a reaction conducted in a single crystal. Only for such reactions proceeding homogenously, we can have reflections of good quality for structure analysis. During the many experiments carried out by us in the past, we noticed that homogeneous photochemical reactions are most probable to proceed in crystals of smaller sizes. Such information was also given independently in literature [19]. Taking into account both aspects, we advise to select single crystals of intermediate thickness: not too thin in order to have strong reflections and not too thick to conduct reactions in a homogenous way. Such crystals were also chosen by us for the studies of structures in this paper.

In order to evaluate the homogeneity of the photochemical reaction conducted in the studied crystal, we applied the Johnson–Mehl–Avrami–Kolmogorov (JMAK) method [20–23]. According to it, the arrangement of molecules in the crystal is described by the equation:

$$P = 1 - \exp[-(kt)^n], \quad (1)$$

where P is the content of product molecules in the crystal, k is the rate constant of the reaction in the crystal, t is the time of irradiation of the crystal, n is the component describing the homogeneity of the reaction.

The values of 2, 3 or 4 for the n constant mean nuclei growth in 1, 2 or 3 directions, respectively. For the homogeneous course of a reaction, the parameter $n = 1$. The values of $n < 1$ can indicate a decrease of reaction rate along with time of irradiation [24]. The JMAK method was applied to several photochemical reactions in crystals [23–30].

In the case of compound **1** and the crystal depicted in Fig. 3d, the n parameter is 0.7, which indicates that the reaction was conducted in a homogeneous way. The reaction rate constant calculated for this crystal on the grounds of the above equation was 1.6×10^{-3} s^{-1}.

Conclusions

Most crystals, in which photochemical reactions proceed, diminish their translational order. This phenomenon has the impact on a decrease of quality of diffraction patterns of single crystals and quality of determined crystal structures. We studied the influence of different external stimuli on the reduction of diffracting power of crystals in the case of methyl 2-{[4-(2,4,6-triisopropylbenzoyl)benzoyl]amino}-3-phenylpropanoate. We observed that there is no correlation between the energy of UV–vis radiation applied to induce the photochemical reaction and the degree of the decrease of crystal diffracting power. We also quantitatively demonstrated a relationship between the reduction of the crystal diffracting power and the content of reactant

molecules in the crystals and quantitatively demonstrated that reactant molecules are responsible for the reduction of crystal diffracting power in the case of the photochemical reaction. In the case of the studied compound and the applied experimental conditions we showed that some change in temperature does not influence the degree of the decrease of the crystal diffracting power. The reaction at the higher temperature was conducted by us in a homogeneous way, however, this was also influenced by the crystal being of a rather small thickness.

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